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(51) International Patent Classification : C12N 15/52, 9/16, C07K 16/40, C12N 11/14, C12Q 1/42, A61K 38/43	A3	(11) International Publication Number: WO 98/04712 (43) International Publication Date: 5 February 1998 (05.02.98)
(21) International Application Number: PCT/US97/13016 (22) International Filing Date: 24 July 1997 (24.07.97) (30) Priority Data: 08/685,992 25 July 1996 (25.07.96) US (71) Applicant: COLD SPRING HARBOR LABORATORY [US/US]; 1 Bungtown Road, Cold Spring Harbor, NY 11724 (US). (72) Inventors: TONKS, Nicholas; 3 Arrowhead Place, Huntington, NY 11743 (US). FLINT, Andrew, J.; 22711 14th Place West, Bothell, WA 98021 (US). (74) Agents: GRANAHAH, Patricia et al.; Hamilton, Brook, Smith & Reynolds, P.C., Two Militia Drive, Lexington, MA 02173 (US).		(81) Designated States: CA, JP, MX, European patent (AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE). Published <i>With international search report.</i> <i>Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.</i> (88) Date of publication of the international search report: 12 March 1998 (12.03.98)
(54) Title: SUBSTRATE TRAPPING PROTEIN TYROSINE PHOSPHATASES (57) Abstract Novel protein tyrosine phosphatases in which the invariant aspartate residue is replaced with an alanine residue and which bind to a tyrosine phosphorylated substrate and are catalytically attenuated are described. Also described are methods of identifying tyrosine phosphorylated proteins which complex with the described protein tyrosine phosphatases.		

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INTERNATIONAL SEARCH REPORT

Intern nal Application No
PCT/US 97/13016

A. CLASSIFICATION OF SUBJECT MATTER

IPC 6 C12N15/52 C12N9/16 C07K16/40 C12N11/14 C12Q1/42
A61K38/43

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 6 C12N C07K C12Q A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	J.W. ECKSTEIN ET AL.: "Identification of an essential acidic residue in Cdc25 protein phosphatase and a general three-dimensional model for a core region in protein phosphatases." PROTEIN SCIENCE, vol. 5, no. 1, January 1996, pages 5-12, XP002051424 see figure 4	1,2,4-10
A	Q. YANG ET AL.: "Cloning and expression of PTP-PEST." THE JOURNAL OF BIOLOGICAL CHEMISTRY, vol. 268, no. 9, 25 March 1993, pages 6622-6628, XP002034265 cited in the application see figure 2	

☒ Further documents are listed in the continuation of box C.

☐ Patent family members are listed in annex.

* Special categories of cited documents:

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- *E* earlier document but published on or after the international filing date
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T later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

X document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

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Date of the actual completion of the international search

9 January 1998

Date of mailing of the international search report

03.02.98

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INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 97/13016

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	Q. YANG ET AL.: "Cloning and expression of PTP-PEST." THE JOURNAL OF BIOLOGICAL CHEMISTRY, vol. 268, no. 23, 15 August 1993, page 17650 XP002051443 cited in the application see the whole document ---	
A	Z. JIA ET AL.: "Structural basis for phosphotyrosine peptide recognition by protein tyrosine phosphatase 1B." SCIENCE, vol. 268, 23 June 1995, pages 1754-1758, XP002051425 cited in the application see the whole document ---	
A	D.L. BRAUTIGAN ET AL.: "Serine phosphorylation of protein tyrosine phosphatase {PTP1B} in HeLa cells in response to analogues of cAMP or diacylglycerol plus okadaic acid." MOLECULAR AND CELLULAR BIOCHEMISTRY, vol. 127/128, 1993, pages 121-129, XP002051426 see the whole document ---	
A	A.J. GARTON ET AL.: "PTP-PEST: a protein tyrosine phosphatase regulated by serine phosphorylation." THE EMBO JOURNAL, vol. 13, no. 16, 1994, pages 3763-3771, XP002051427 cited in the application see the whole document ---	
A	A.J. FLINT ET AL.: "Multi-site phosphorylation of the protein tyrosine phosphatase, PTP1B: identification of cell cycle regulated and phorbol ester stimulated sites of phosphorylation." THE EMBO JOURNAL, vol. 12, no. 5, 1993, pages 1937-1946, XP002051428 cited in the application see the whole document ---	
P,X	A.J. FLINT ET AL.: "Development of "substrate-trapping" mutants to identify physiological substrates of protein tyrosine phosphatases" PROC. NATL. ACAD. SCI. USA, vol. 94, March 1997, pages 1680-1685, XP002051429 see the whole document ---	1-12
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INTERNATIONAL SEARCH REPORT

Initial Application No
PCT/US 97/13016

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P,X	A.J. GARTON ET AL.: "Identification of p130cas as a substrate for the cytosolic protein tyrosine phosphatase PTP-PEST." MOLECULAR AND CELLULAR BIOLOGY, vol. 16, no. 11, November 1996, pages 6408-6418, XP002051430 see the whole document	1-12
P,X	--- B.L. SEELY ET AL.: "Protein tyrosine phosphatase 1B interacts with the activated insulin receptor." DIABETES, vol. 45, no. 10, October 1996, pages 1379-1385, XP002051432 see the whole document	1-12
P,X	--- F. LIU ET AL.: "Direct binding of a proline-rich region of protein tyrosine phosphatase 1B to the Src Homology 3 Domain of p130 cas" THE JOURNAL OF BIOLOGICAL CHEMISTRY, vol. 271, no. 49, 6 December 1996, pages 31290-31295, XP002051433 see the whole document	1-12
A	--- D. BARFORD ET AL.: "Crystal structure of Human protein tyrosine phosphatase 1B." SCIENCE, vol. 263, 11 March 1994, pages 1397-1403, XP002051434 see the whole document	
A	--- H. SUN ET AL.: "MKP-1 {3CH134}, an immediate early gene product, is a dual specificity phosphatase that dephosphorylates MAP kinase in vivo." CELL, vol. 75, 5 November 1993, pages 487-493, XP000611983 cited in the application see the whole document	

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 97/13016

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
see FURTHER INFORMATION sheet PCT/ISA/210
2. ☐ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Remark : Although claims 13 to 20 are directed to a method of treatment of the human/animal body , the search has been carried out and based on the alleged effects of the compound/composition.